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Medulloblastoma in adults. A case presentation and review of the literature

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Summary

Aim	The aim of this article is to present a case of medulloblastoma in an adult patient aged 46 and the problems associated with its treatment.
Case Description	The authors present a case of medulloblastoma in a 46-year old male patient. The tumour, which is typically identified in childhood, is very rare in adults. The incidence rate, in individuals older than 16 years of age, is 0.05 per 100,000.
Results	The patient was subjected to combined therapy consisting of surgery and subsequent radiotherapy. This choice of management was successful – the patient has been followed up since the completion of therapy and no relapses have been noted.
Conclusions	Based on this particular case, and the current literature, the authors discuss contemporary management methods in medulloblastoma.
Key words	adult • medulloblastoma • radiotherapy

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BACKGROUND

Medulloblastoma accounts for 20% of brain tumours arising in childhood [1]. Peak incidence occurs between the 5 and 10 year of life. Medulloblastoma is very rare in adults and reports of its occurrence worldwide are scarce.

The most common site for medulloblastoma development is the cerebellar vermis. From this location the tumour penetrates into the fourth ventricle, resulting in abnormalities in the flow of cerebro-spinal fluid. Often the tumour surrounds and infiltrates the fourth ventricle, retracting the brachium pontis and subsequently spreading towards the ventricular floor. Spreading along the cerebro-spinal fluid routes, medulloblastoma may become disseminated within the central nervous system in 10–30% of pediatric patients.

Medulloblastoma belongs to the PNET group of tumours that originate from primitive, neuroepithelial cells.

The tumour has two histological variants: classic and desmoplastic. The desmoplastic form is found in 20–40% of adult cases and in 10% of pediatric patients. [2–4] Some authors believe that – after comprehensive therapy – the prognosis in medulloblastoma is more favorable in adults than in children [2].

Therapeutic management of medulloblastoma consists of an as-radical-as-possible excision of the tumour mass, followed by irradiation.

In children, chemotherapy is also applied, though routine chemotherapy in adult patients is still a matter of controversy in view of the very low incidence of this malignancy, the resultant problems in finding a uniform group of patients for clinical trials, and the slightly different course of the disease as compared to children.

AIM

The aim of this article is the presentation of a case of medulloblastoma in an adult patient aged 46 years, and the problems associated with its treatment.

CASE PRESENTATION

A 46-year old male had been complaining, for 2 years, of severe, periodic headaches and dizziness, mostly in the afternoon. Diagnostic studies were

carried out in the Departments of Neurosurgery and Neuropathology at the Jagiellonian University of Cracow. Computed tomography and magnetic resonance imaging of the head showed a tumour located in the posterior cranial fossa (Figure 1A,B). The patient was operated and a tumour of the vermis and cerebellar hemispheres was totally excised. Histopathologically the tumour was diagnosed as medulloblastoma. After surgery, the patient awoke but subsequently lost consciousness. Computed tomography revealed an epidural haematoma, which was promptly removed. One month later the patient was readmitted, owing to a considerable collection of cerebrospinal fluid at the surgical site, causing extracranial bulging. The patient was operated and an Orbis-Sigma ventriculo-peritoneal valve was implanted. Following the shunt, the clinical and neurological status of the patient was found to be good. Subsequently, the man was referred to the Department of Oncology, Jagiellonian University of Cracow, where he was qualified for adjuvant radiotherapy. Radiation therapy was planned using a three-dimensional computer-aided planning system. CT images were taken at 15mm intervals in the spinal cord area and every 5mm for the cranial area (Figure 2). Next, PTV and the volume of tumour bed after surgery, with a 3cm margin, were outlined. Individual blocks, shielding healthy tissues, were planned and dose volume histograms were calculated. Irradiation was performed using an X-ray beam generated by a linear accelerator at the Radiotherapy Unit, University Children's Hospital of Cracow. A photon beam was applied to the brain, using the two opposing fields technique with shielding to the bones of the face, as well as to the spinal cord employing the three posterior fields technique, with a moving gap between fields. The dose was 3500cGy administered in 21 fractions. A boost of 2000cGy divided into 11 fractions was applied to the posterior cranial fossa, making the total dose 5500cGy. For this patient, no multi-field conformal techniques, for increasing the dose delivered to the tumour bed, were used. This was due to the fact that the PTV volume, including the tumour bed with a 3cm margin, seemed to be quite large and choosing a more complicated radiotherapy technique than the one used would not help with sparing the hypothalamic-pituitary system or temporal lobes. In view of the signs of intracranial pressure, anti-edematous agents were administered. The patient tolerated the therapy fairly well. At present, two years after completion of treatment his clinical and neurological status is good and he attends follow-up examinations at the Departments of Oncology and Neurology.

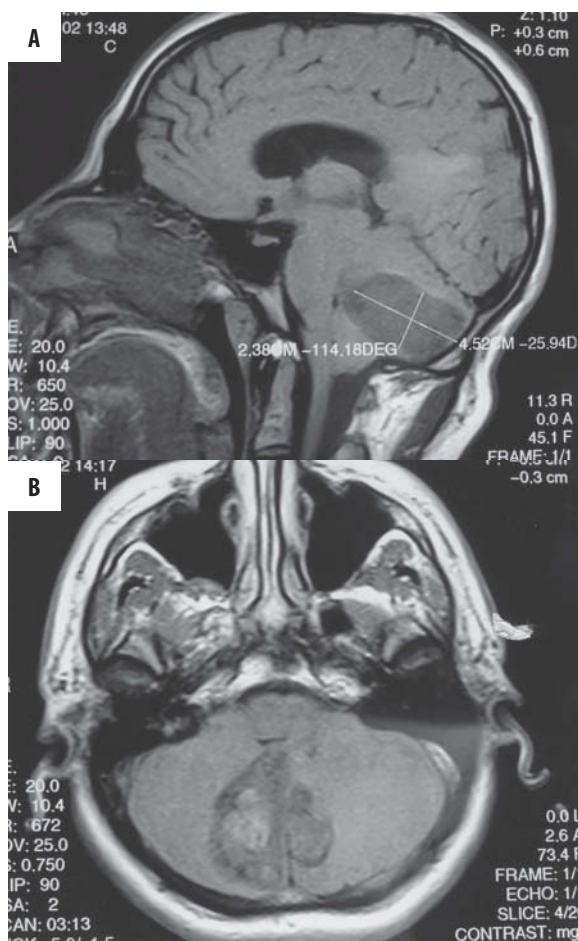


Figure 1A,B. Sagittal and axial T1 weighted MRI. A large tumour of the posterior cranial fossa localized in the vermis and cerebellar hemispheres.

DISCUSSION

Medulloblastoma is counted among childhood tumours. Its incidence among adults is low; the annual morbidity rate being approximately 0.05 per 100 000 [1].

The mean age of such adult patients is approximately 25 years (22.4–34.1). Cases in patients older than 40 are very rare. Our patient was 46 years old at the time of diagnosis.

The tumour was located in the vermis as is often the case in children, although in adults it is more often situated in the cerebellar hemispheres [3–5].

Standard management in adults lies in maximally radical surgery with subsequent irradiation. The elevated risks from surgery should however be taken into account in some cases, particularly those involving large tumours. Postoperative

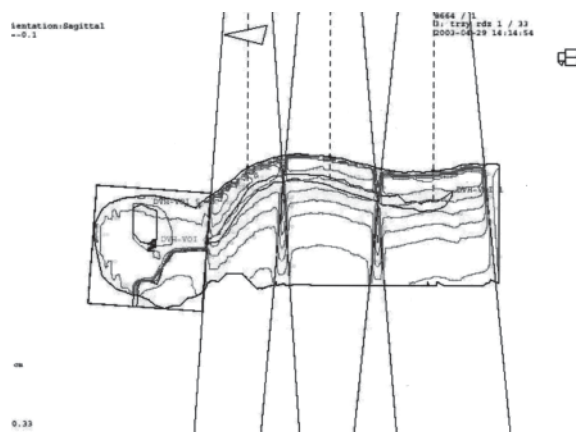


Figure 2. Irradiation of the central nervous system. Dose distribution.

complications such as haematoma or cerebrospinal circulation disturbances can affect outcome. Besides, radiotherapy may be postponed owing to additional neurosurgical procedures – haematoma removal, or cerebrospinal fluid shunting. In our case we experienced the mentioned complications, which affected neither neurological outcome, nor significantly postponed further treatment. In 1920, Cushing was the first to report surgical results obtained in children with medulloblastoma; the author managed to achieve 3-year survival in only one of 61 patients [6]. Between the years 1932 and 1947, Patterson employed postoperative radiotherapy of the entire central nervous system, achieving 5-year survival in five of 12 children [6].

At present, the standard of management, both in older children and in adults, is combined therapy consisting of a maximally radical operation followed by adjuvant irradiation of the entire central nervous system. Irradiation uses doses of up to 3500cGy and the dose to the posterior cranial fossa is subsequently increased, reaching an accumulated dose of 5500cGy.

To achieve this purpose, a photon beam is applied to the entire brain and cervical spine up to the C3–C5 level using the two opposite fields technique and shielding the facial skeleton; the beam is also applied to the spinal cord using the two or three posterior fields technique with a moving gap mid-treatment, the dose being 3500cGy divided into 21 fractions; additionally, a dose of 2000cGy divided into 11 fractions is applied to the posterior cranial fossa until a cumulative dose of 5500cGy is reached. In certain cases, where the tumour was small and radically removed without

risk of relapse on the field border, it is possible to use conformal techniques for the tumour bed with a 3cm margin instead of posterior cranial fossa irradiation, which allows for sparing of the hypothalamus and pituitary gland. The best solution is delineation of the tumour volume before surgery, with patient immobilized in the treatment position. However, on rare occasions in which intracranial hypertension is observed, the clinical status of the patient forces immediate surgical intervention.

In the late sixties, chemotherapy was first introduced for children. Based on multi-center clinical trials, chemotherapy has been demonstrated to improve therapeutic results in children with high-grade disease in so-called high-risk groups [7]. In low-risk groups, when tumours can be radically excised, their size is below 3cm and there are no metastases, the role of chemotherapy continues to be controversial [7].

In Poland, a protocol approved by the Polish Pediatric Group for CNS tumour treatment is applied; before radiotherapy in low-risk groups: vincristine, etoposide, carboplatin are given, alternating with cyclophosphamide, and in high-risk groups: ifosfamide is used instead of cyclophosphamide and cisplatin replaces carboplatin. After radiotherapy – 6 to 8 courses of cisplatin, vincristine and CCNU are used. Routine postoperative chemotherapy is applied in younger children, below 3 years of age, while radiotherapy is delayed until the child is at least three years old. In this group of patients, in view of the incomplete development of their central nervous systems, post-irradiation complications are the most severe.

Studies on introducing chemotherapy to the management of adult patients have not produced the expected results. The results were from studies into concurrent, or more frequently adjuvant chemotherapy, according to different protocols e.g. lomustine, vincristine and procarbazine (2,3), vincristine, lomustine and carmustine or ifosfamide, cisplatin and vincristine (1), weekly vincristine during radiotherapy, followed by 8 cycles of cisplatin, lomustine and vincristine or, according to the Pediatric Oncology Group guidelines, cisplatin/etoposide and cyclophosphamide/vincristine followed by irradiation [8] and, in the poor-risk group adjuvant therapy with lomustine, vincristine and cisplatin [7].

Some authors report the beneficial effects of such therapy on therapeutic results [9,10], though the

majority of investigators have failed to demonstrate any statistically significant differences in the total and event-free survival rates [1,11–13]. In some reports the results were in fact poorer owing to an increased incidence of post-chemotherapy complications in adults in comparison to pediatric patients [1]. Investigations on the use of chemotherapy in adults continue, including megachemotherapy with hematopoietic stem cell implantation, though the results remain controversial.[14].

The management of adult patients with medulloblastoma is, therefore, still based on surgery, as radical as possible, supplemented by irradiation of the entire central nervous system with increased doses applied to the site of the removed tumour.

When the above-described management is applied, the results achieved in adults with medulloblastoma are slightly better than in children [2]. As in the case of pediatric patients, adults may also be divided into low-risk and high-risk groups [15,16]. Event-free five-year survival rates amount to 40–65%, while ten-year survival is seen in approximately 20–40% of patients [10,12,13,15]. Total five-year survival rates are approximately 60–80%, while ten-year survival is observed in 40–50% of cases [3,10,12,17,18]. In low-risk groups of children, event-free five-year survival occurs in 85%, while in high-risk groups the corresponding rate is up to 50%. Ten-year survival is seen in approximately 30%. The outcome in adult patients shows considerable inter-centre variation and the reporting of precise data is hindered by the low numbers of investigated patients.

Relapses in adults occur after a mean period of 30–40 months, following the completion of therapy [1,13].

The most common site for relapses, in both children and adults, is the posterior cranial fossa [1,3,8,15,16,19]. The dissemination of medulloblastoma along the cerebro-spinal fluid routes is slightly less common and is usually observed in cases of recurrent tumour at the original surgical site [3]. Metastases to remote sites such as the bones, lungs, pancreas and lymph nodes are sporadic. The mean survival time after detection of a relapse, and associated emergency treatment, is 77 weeks (range of 44 to 89 weeks) [3,20]. Early detection of tumour recurrence has a positive effect on therapeutic results. Some reports show that approximately one half of patients achieve remission following a second course of treatment [20].

The most commonly applied management, in cases of relapse in children, is second-line chemotherapy, or megachemotherapy, using haematopoietic stem cell implantation. The outcome is poor and the majority of patients do not survive past 24 months. In adult patients with relapses one may consider the use of chemotherapy when chances of success from irradiation have already been exhausted [14]. Re-operation of the tumour is controversial, especially in the irradiated region. The outcome is positively affected by low staging of clinical disease advancement prior to treatment, desmoplastic histological tumour type, completeness of surgery, a total dose - applied to the entire central nervous system - of at least 35Gy (and at least 54Gy to the posterior cranial fossa) [1,2,19,21], and – according to some investigators – female sex and older age [4,22].

Data on the incidence of medulloblastoma in adults is scarce. Thus, it is difficult to collect a uniform group of patients. In Poland, Skolyszewski and Gliński described a series of 13 adult patients with medulloblastoma, ranging in age from 16 to 52 years, with a mean age of 22.4 years. The authors achieved event-free five-year survivals in 62% of cases [23]. Based on data from the literature regarding the incidence of medulloblastoma in adults, one may claim that the 46-year old patient we describe here is a very rare case [24,25]. We assume that the applied therapeutic method was optimal, though ultimate evaluation requires prolonged follow-up.

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